**2445-Pos Board B137**
**Parsing the Contributions of Polypeptide Backbones and Sidechains to Denaturation in Concentrated Aqueous Solutions of Urea and Guanidinium Chloride**
**Alex S. Holehouse**[1], Nicholas Lyle[2], Andreas Vitalis[3], Devarajan Thirumalai[4], Rohit V. Pappu[1].
[1]Biomedical Engineering, Washington University in Saint Louis, St Louis, MO, USA, [2]Partek Incorporated, St Louis, MO, USA, [3]Department of Biochemistry, University of Zurich, Zurich, Switzerland, [4]Institute for Physical Sciences and Technology, University of Maryland, College Park, MD, USA.
The mechanistic details of protein denaturation are relevant for understanding the nature of the collapse transition that is induced by dilution from denaturing to predominantly aqueous solutions. Concentrated solutions of urea and GdnCl are thought to be good solvents for generic proteins. Here we report results from a series of systematic molecular dynamics simulations. We show that the solvent quality of a denaturing solution depends on the chemical details of the polypeptide system. Polyglycine prefers collapsed states in highly concentrated aqueous solutions of GdnCl, implying that these solvents are poor solvents for polypeptide backbones. The induction of chain expansion in 6 M GdnCl requires the addition of specific categories of sidechains including those with aromatic groups, primary amides, and charged groups. Polyglycine expands in highly concentrated aqueous solutions of urea. However, we show that intra-chain and chain-solvent interactions are almost perfectly counterbalanced in 8 M urea, implying that these conditions are theta solvents for generic polypeptide backbones. The degree of chain expansion can be enhanced in urea by the addition of sidechains that interact favorably with urea molecules. Polypeptide backbones and sidechains contribute to chain expansion through preferential interactions with denaturant molecules in 6 M GdnCl and 8 M urea, although the contributions from sidechain and backbone specific interactions are different in the two milieus. Importantly, we observe that the degree of expansion falls short of the upper limit that is achievable for self-avoiding random walks. This implies that the degree of chain expansion can be sequence-specific and be impacted by residual intra-chain attractions. This should influence the details of the collapse transition upon dilution from denaturants.

**2446-Pos Board B138**
**The Structure of the β-Casein Phosphopeptide Consists of Two Independent Intrinsically Disordered Domains**
**Muhammad A. Naqvi**[1], Sarah Rauscher[2], Régis Pomès[2], Dérick Rousseau[3].
[1]Ryerson University, Richmond Hill, ON, Canada, [2]Molecular Structure and Function, Hospital of Sick Children, Toronto, ON, Canada, [3]Ryerson University, Toronto, ON, Canada.
The determination of the β-casein phosphopeptide 1-25 (β-CPP) structure has to date remained elusive, yet has important implications for calcium binding and cellular transduction as well as the mechanisms involved with dental remineralization. Though its high net charge of 13e suggests that it is an intrinsically disordered peptide (IDP), there is significant disagreement regarding its degree of disorder. The structure of β-CPP was examined via molecular dynamics (MD) simulations to investigate its degree of disorder. One hundred independent MD simulations for a cumulative time of 30 μs were conducted in explicit water with 0.1 M sodium chloride. The results showed that β-CPP adopts an ensemble of collapsed conformations ($Rg=8.61\pm0.06$ Å) that are stabilized by hydrogen bonding (HB) as well as ionic interactions. The HB contact map showed a lack of interaction between the peptide's head (RELEELNVPGEIVES) and tail (SSSEESITR) domains suggesting that they were conformationally independent. Significant backbone HB interactions were observed amongst the amino acids within each domain, further indicating that they were disordered. By determining the conformational ensemble of this peptide, this study has successfully shown that β-CPP is an IDP with two independent, intrinsically disordered domains.

**2447-Pos Board B139**
**MD Simulation Trajectories of Multiple Intrinsically Disordered Proteins Reveal Order to Disorder Transitions that Bear Functional Significance**
Tasneem Ali, Mattaparthi Venkata, Satish Kumar, Saurabh Basu, **Rajaram Swaminathan**.
Indian Institute of Technology Guwahati, Guwahati, India.
Intrinsically disordered proteins (IDPs) explore a dynamic ensemble of conformations and yet retain a functional role inside the cell. However, the correlation of backbone chain dynamics of an IDP correlated with its cellular function is not fully understood. Here in this work we analyze the MD simulation trajectories (12500 timesteps of total 10 nanosecond duration) of one ordered protein (catalytic domain of MutY from E. Coli, pdb code: 1MUN), one partially ordered protein (Apoptosis regulator Bcl-xL, 1LXL) and four IDPs (Brak/CXCL14, 2HDL; sub-domain of staphylococcal nuclease, 2SOB; F6 subunit of ATP synthase, 1VZS and Tyrosyl tRNA synthestase, 1JH3). The analysis included distance variations between chosen multiple points in the protein backbone, probability distributions of the measured distances and their velocities, and full width half maxima of these probability distributions. The results from the analysis yielded a quantitative measure of dynamics at loop regions in comparison to helix and strand regions. In addition the distance probability distributions of loop regions in IDPs specifically displayed multimodal character indicating distinct preferences for certain distances. This was in contrast to velocity probability distributions which were always of unimodal nature for all the six proteins. Further, we attempted to quantify the randomness in disordered chain dynamics by computing the Boltzmann entropy for all c-alpha atoms in each of the proteins. This entropy value for a given c-alpha atom correlated with its wandering ability in space. Disorder-order transition regions were spotted from the created protein movies and analyzed quantitatively by constructing Ramachandran plots for those regions across all time steps. Such regions included lysine residues previously speculated to be involved in post-translational modifications in F6 unit of ATP synthase and RNA binding domain in Tyrosyl tRNA synthestase.

**2448-Pos Board B140**
**Physical Bioinformatics Applied to Intrinsically Disordered Nucleoporin Sequences Reveals Universal Functional Features**
**David Ando**[1], Michael Colvin[2], Michael Rexach[3], Ajay Gopinathan[1].
[1]Physics, UC Merced, Merced, CA, USA, [2]Chemistry, UC Merced, Merced, CA, USA, [3]Molecular, Cell, and Developmental Biology, UC Santa Cruz, Santa Cruz, CA, USA.
Bioinformatics of disordered proteins is especially challenging given high mutation rates for homologous proteins and that functionality may not be strongly related to sequence. We introduce a novel form of bioinformatic analysis, which can be applied to disordered proteins, based on the spatial clustering of physically relevant features such as binding motifs and charges. We apply this technique on thousands of disordered Nuclear Pore Complex (NPC) FG motif containing proteins (FG nups) to elucidate the elusive biophysical mechanism by which FG nups regulate nucleocytoplasmic transport. Our analysis reveals a set of highly conserved spatial features in the sequence structure of individual FG nups, such as the separation, localization, and ordering of FG motifs and charged residues along the protein chain. These conserved features provide insight into the functioning of the pore and strongly constrain current models. Additionally this method allows us to identify potentially functionally analogous disordered proteins across distantly related species.

**2449-Pos Board B141**
**Extensive use of Host-Mimicking Motifs Supports Complex Regulation of Viral Proteins**
**Tzachi Hagai**[1], Raul Andino[1], Madan M. Babu[2], Ariel Azia[3].
[1]University of California, San Francisco, San Francisco, CA, USA, [2]MRC-Laboratory of Molecular Biology, Cambridge, United Kingdom, [3]Bar Ilan University, Ramat Gan, Israel.
In order to successfully replicate, viruses engage in complex interactions with their hosts. Small motifs that are used by eukaryotes in cellular regulation are thought to be mimicked by viral proteins to support their interactions with the host. Due to experimental difficulties, comprehensive analyses of which viruses and what proteins use motifs, as well as their role in modulating host-virus interactions, has so far been hampered. Here, we analyze a large set of viral proteins representing all viral types and most viral families. We show that the occurrence of motifs varies greatly among viral families and protein types. Some proteins seem to use motifs sparsely whereas others contain numerous motifs that co-occur in a manner that facilitates multiple coordinated interactions. Our results reveal a surprising complexity of combinatorial regulation of viral proteins, characteristic of tightly-regulated eukaryotic proteins, to achieve an efficient and finely-tuned infection.

## Transcription

**2450-Pos Board B142**
**Mechanism of Transcriptional Bursting in Bacteria**
**Shasha Chong**[1], Chongyi Chen[1], Hao Ge[2], X. Sunney Xie[1,2].
[1]Harvard University, Cambridge, MA, USA, [2]Peking University, Beijing, China.
Many single-cell experiments have shown that transcription of highly expressed genes occurs in stochastic bursts in bacteria. Here we present the mechanism of this ubiquitous phenomenon. We develop a high-throughput in vitro single-molecule assay to observe real-time transcription on individual DNA templates. Using this assay, we demonstrate that positive supercoiling buildup on the DNA by transcription slows down transcription elongation